

DEC 29 2003

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Faxed: December 29, 2003
Applicant: Carl T. Wittwer
Invention: AUTOMATED ANALYSIS OF REAL-TIME NUCLEIC ACID AMPLIFICATION
Serial No.: 10/074,169
Filed: February 12, 2002
Docket: 7475-70049

☒ Response to Restriction Requirement (5 pages)

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(317) 231-7433 Fax**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Group: 1655

Confirmation No.: 5884

Application No.: 10/074,169

Invention: AUTOMATED ANALYSIS OF
REAL-TIME NUCLEIC ACID
AMPLIFICATION

Applicant: Carl T. Wittwer

Filed: February 12, 2002

Attorney Docket: 7475-70049

Examiner: Fredman

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Trademark Office, centralized fax number 703-872-
9306on December 29, 2003Joyce Hamilton
(Signature)Joyce Hamilton
(Printed Name)**Response to Restriction Requirement**Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed on November 28, 2003, the Applicant respectfully requests entry of the following amendments and consideration of the following remarks. The Applicant believes that no additional fees are required with this response. If fees are required, it is respectfully requested that the fees be charged to the account of Barnes & Thornburg, Deposit Account No. 10-0435, with reference to our matter 7475-70049.

IN THE CLAIMS:

1. (original) A method for determining the presence of a nucleic acid in a sample comprising the steps of
providing a fluorescent entity capable of indicating the presence of the nucleic acid and capable of providing a signal related to the quantity of the nucleic acid,
amplifying the nucleic acid through a plurality of amplification cycles in the presence of the fluorescent entity,
measuring fluorescence intensity of the fluorescent entity at each of the plurality of amplification cycles to produce a fluorescent value for each cycle related to the quantity of the nucleic acid present at each cycle,
generating a plot wherein the fluorescent values are recorded for each amplification cycle,
performing a confidence band analysis on the plot to generate a positive or negative call, and
if the call is positive, confirming the positive call by a melting temperature analysis.
2. (original) The method of claim 1 wherein the confidence band analysis is performed by
calculating slopes of segments of the plot using a plurality of the fluorescent values,
using the segment slopes of the plot to establish a baseline fluorescence region by generating a slope value for each of a plurality of the amplification cycles, and establishing the baseline fluorescence region comprising an interval of cycles that includes the amplification cycle with the slope value having an absolute value closest to zero, and
making the positive or negative call based on whether the fluorescence value during a selected amplification cycle is outside the baseline fluorescence region.
3. (original) The method of claim 2 wherein the baseline fluorescent region is established without the use of an internal standard.

4. (original) The method of claim 1 wherein the melting temperature analysis is performed by
 - obtaining a melting profile,
 - determining the minimum or maximum of the first derivative to generate a T_m value, and
 - comparing the T_m value with the known T_m of the target analyte.
5. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence between extension and denaturation during one of the amplification cycles.
6. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence between annealing and denaturation during one of the amplification cycles.
7. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence in a separate melting process subsequent to amplification.
8. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence at 0.1°C temperature increments.
9. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence at temperature increments of greater than 0.1°C.
10. (original) An automated method for determining the presence of a nucleic acid comprising the steps of
 - placing a sample into a container containing a fluorescent entity capable of indicating the presence of the nucleic acid and capable of providing a signal related to the quantity of the nucleic acid,
 - placing the container into a device for amplifying the nucleic acid through a plurality of amplification cycles in the presence of the fluorescent entity,
 - measuring fluorescence intensity of the fluorescent entity at each of the plurality of amplification cycles to produce a fluorescent value for each cycle related to the quantity of the nucleic acid present at each cycle,
 - generating a plot wherein the fluorescent values are recorded for each amplification cycle,

calculating slopes of segments of the plot using a plurality of the fluorescent values,

using the segment slopes of the plot to establish a baseline fluorescence region by generating a slope value for each of a plurality of the amplification cycles, and establishing the baseline fluorescence region comprising an interval of cycles that includes the amplification cycle with the slope value having an absolute value closest to zero,

outputting a positive result if the fluorescence value of a selected amplification cycle is outside the baseline fluorescence region, and

confirming the positive result by melting temperature analysis.

11-13. (cancelled)

REMARKS

The office action mailed on November 28, 2003 required restriction of the 13 pending claims of the captioned application to one of 2 groups. The claim groups identified by the Examiner are as follows:

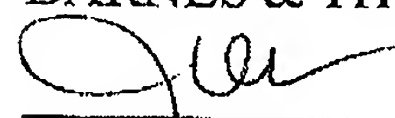
Group I: claims 1-10, drawn to a method of detection of nucleic acid.

Group II: claims 11-13, drawn to a PCR apparatus.

Applicant elects Group I. Claims 11-13 have been canceled.

Applicants respectfully request allowance of the pending claims and passage of the application to issuance.

Respectfully submitted,
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INDS02 JTP 625359v1